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PATHOGENESIS OF ACUTE PULMONARY EDEMA IN SURGERY OF PULMONARY TUBERCULOSIS

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I. INTRODUCTION

Backward heart failure due to weakness of the left ventricle was long thought to be the chief cause of acute pulmonary edema.

In surgery for pulmonary tuberculosis there are certainly cases of pulmonary edema which can be explained by this theory, but, on the other hand, we sometimes meet cases in which the signs of pulmonary edema precede that of heart failure. How are these cases to be explained? At least the theory of the backward heart failure seems to fail in these instances.

Recently Altschule¹⁾ gave his view on this matter. He concluded that the cause of pulmonary edema was an unbalance between transudation from pulmonary vessels and absorption of the transudate into lymph canals.

This theory interested us so much that we began our researches by rediscussing it. But as we proceeded we found out an important fault in this theory, too.

Histologically examined, the main changes in edematous lung occur in the periarterial connective tissues, the interstitial tissues of the alveolar region and in the alveolar spaces. In the periarterial connective tissues there are found the two phenomena as Altschule referred to, transudation and absorption. In the alveolar region, however, there are no lymph canals, and therefore there can be no absorption into lymph canals. Hence, we are afraid, Altschule's theory loses its validity, too.

Thus the theories so far presented are not satisfactory, and we, through clinical and experimental researches, have got a conclusion that will explain the process of pulmonary edema.

In the following we are going to report our researches.

II. CLINICAL STUDY

In our institute and its affiliated hospital we have experienced 33 cases of acute pulmonary edema during or after operations (Table 1). Studying them we can reduce the thought-to-be inducing factors into two categories. One is ventilatory insufficiency and other is bleeding of a large amount of over-transfusion and

Table 1. Operation methods performed

Operation methods	Cured	Dead	Total
Pneumonectomy	1	7	8
Lobectomy (including segmental resection)	8	9	17
Thoracoplasty (including Cavernostomy)	3	5	8

Table 2. Inducing factors of acute pulmonary edema in pulmonary tuberculosis surgery

- I) Ventilatory insufficiency
 - (1) Mechanical effects of ventilatory insufficiency
 - (2) Anoxia
 - (3) Hypercapnia
- II) Hemorrhage
 - (1) Acute bleeding of a large amount
 - (2) Over-transfusion and -infusion after bleeding

Table 3. Initial symptoms of pulmonary edema (in 33 cases)

Bloody and frothy sputa.....	24
Wet rales.....	21
Cyanosis	16
Dyspnea	11
Hypertension	8
Paradoxical respiration	3
Coma.....	2
Stridor	1
Edema on face	1

-infusion (Table 2). Initial symptoms on the onset are summarized in Table 3. In them hypertension is worth consideration. It was at first thought to be the result of hypercapnia due to the preceding pulmonary edema. But we found that on high CO₂ breathing many tuberculous patients showed an increase of the pulmonary wedge pressure. One of them presented even as high pressure as the colloid osmotic pressure of blood. This means that the retention of CO₂ is not the result but one of the causes of pulmonary edema.

III. EXPERIMENTAL STUDIES

1) Transudation of the blood components from the pulmonary vessels

a) Lymphodynamics in dog's lung

Pulmonary edema, in short, begins with transudation from the pulmonary vessels. Its onset and development are very acute. We wanted, therefore, to observe the entire courses of the changes from the beginning to the end. For this purpose we were at first going to employ Drinker's²⁾³⁾⁴⁾⁵⁾ method: observing the lymphodynamics of dog's lung at the site of the right lymphatic trunk. But this method was not only artificial but also inconvenient because the experiment was performed with the dog's chest opened and under regulated respiration. In

our experiments this method was improved so as to be done with the animal's chest kept unopen. Moreover there was a question in Drinker's method whether the lymphodynamics at the site of the right lymphatic trunk represented directly and exactly the transudation from the pulmonary vessels. Our answer to this question was yes. In the periarterial region there were recognized not only retention of the transudate and bleeding, but also reabsorption of the transudate into the lymph canals nearby so much as to make hemolymph. This phenomenon gives us an affirmative proof for the answer.

During under anesthesia the respiration of the dog was calm, and no remarkable change in lymph flow and protein content of lymph was recognized. As the respiratory frequency increased, lymph flow also increased without any change in the protein content.

On low oxygen breathing of about 10 vol.% O_2 an increase of lymph flow together with a decrease of protein content occurred promptly (Fig. 3). This shows an increased transudation from the pulmonary vessels. These changes reduced their degree gradually and swung down back to the former levels promptly after the room air respiration was recovered. But these both changes occurred to the various degrees under other conditions also, such as high CO_2 breathing of about 10 vol.% CO_2 , bleeding of 20 cc/Kg. Wt. and liquid infusion of 100 cc/Kg. Wt.

Compared with these, under double loaded condition of simultaneous low oxygen and high CO_2 breathing respectively of about 10 vol.% or during low oxygen breathing under any respiratory resistance, lymph flow increased abruptly so much as to make hemolymph and, besides, often did not diminish as time passed and the hemolymph remained as it has been even after the load was removed (Fig. 2). In such a case pulmonary edema was established.

We classified pulmonary edema into four stages according to the degrees of the histologic changes in the alveolar region. But the degree of changes seemed

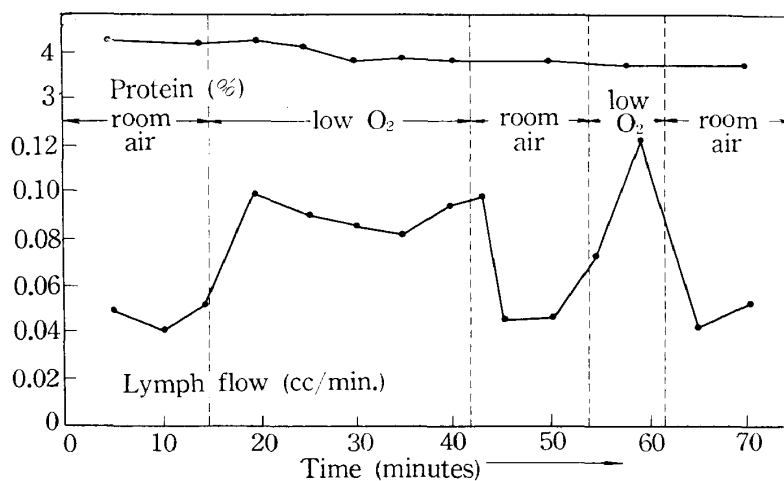


Fig. 1. Effect of low oxygen breathing (9.8 vol.%) upon the pulmonary lymph flow (dog).

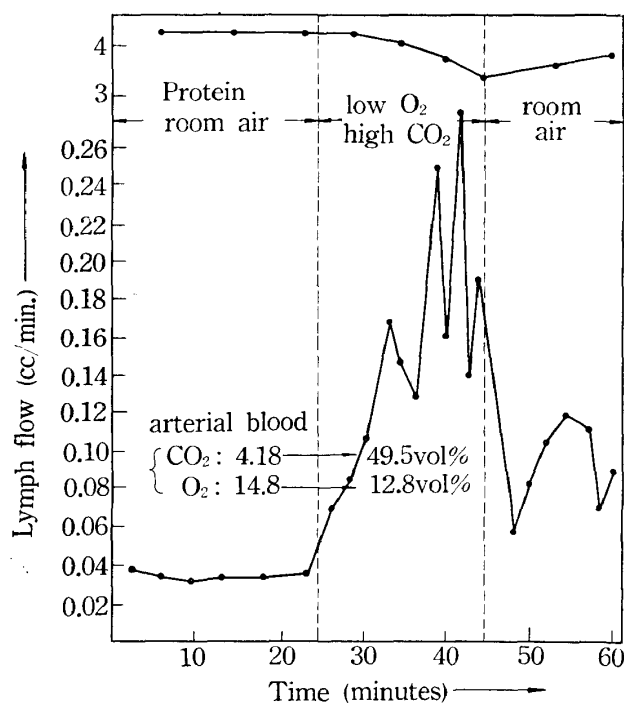


Fig. 2. Effect of simultaneous low oxygen (11.9 vol. %) and high CO_2 (12.7 vol. %) breathing upon the pulmonary lymph flow (dog).

in turn to be grossly determined by sort of the condition loaded. In the case of the single loaded breathing of low oxygen or high CO_2 , there was no change found at all or, if any, of the first or the second stage at most. But under the double loading of simultaneous low oxygen and high CO_2 breathing or under respiratory resistance, changes of the third or the fourth stage, namely the very changes of typical pulmonary edema, were often brought about.

b) Water content of rabbit's lung

All experiments above were performed on dogs. As for rabbits, however, it was difficult to observe the lymphodynamics of the lungs, so instead of that we measured the water content of the organ.

Because the method of measuring it so far used had some faults we have devised a method employing the radioactive isotope P^{32} as a tracer.

The results gained in the experiments on rabbits were rather unexpected. Even under the double loaded conditions as well as under the single, the water content of the lungs was within the normal range, and histologically there was also no or, if any, very slight change of within the second stage. Much the same was true after bleeding or infusion. In these cases the water content of the lungs changed temporarily for a time but by and by returned to the normal value, and the histologic changes were also very slight.

c) Summary of the preceding two sections

Now we can summarize the results of our experiments so far as follows.

(1) No pulmonary edema is caused in lungs of dogs nor rabbits by either low oxygen or high CO₂ breathing of within clinically available vol.% and by venesection (bleeding) or infusion of clinical volume.

(2) Pulmonary edema is caused in lungs of dogs but not of rabbits by the double loading of simultaneous low oxygen and high CO₂ breathing and by anoxia under respiratory resistance.

d) Reserve vessels

Where does this difference as above between the two animals come from? As is well known, somewhat increased pulmonary blood flow or blood volume does not always bring about a rise of the pulmonary arterial pressure. This fact has been explained by assuming that dilation of the vessels and recanalization of the reserve vessels meet enough the increased pulmonary blood flow or volume. The assumption was ascertained to be true by our microscopic observation on the living peripheral pulmonary vessels of rabbits which revealed blood arrests here and there which suggested the existence of reserve vessels.

Injection of adrenalin and physiological saline solution can give rise to a typical pulmonary edema. By a continuous observation through the course we could see a row of changes continuing one after another, in the order of the process recanalization of the reserve vessels, filling up of arterioles, venules and capillaries by erythrocytes and their leakage into the alveolar spaces.

Recanalization of the reserve vessels was demonstrated also under the single loading of low oxygen or high CO₂ breathing, under the double loading of these two conditions and after liquid infusion.

On dogs, however, microscopic observation of the living lungs was not available and we could not but employ Aviado's⁶⁾ method in an attempt to measure

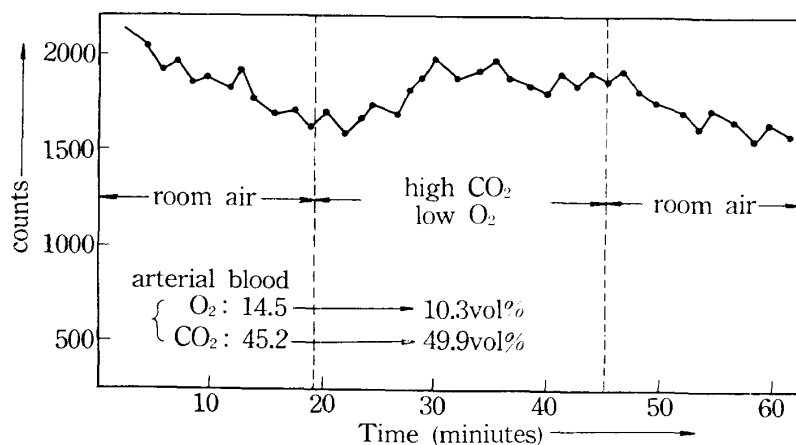


Fig. 3. Pulmonary blood volume under simultaneous low oxygen (9.6 vol. %) and high CO₂ (10.1 vol. %) breathing (dog, measured by P³²).

the blood volume in the alveolar vessels.

Under the single loading of low oxygen or high CO₂ breathing both in the concentration of about 10 vol.%, the count number increased for a short time but soon followed the normal pattern of the decaying curve.

Under the double loading the count number remained increased continuously through the period (Fig. 3). This means in dogs the double loading may cause a lasting unusual dilation of the peripheral pulmonary vessels.

e) Summary of the preceding section

In case when the pulmonary blood flow or volume increases

- (1) The unusual dilation of the peripheral pulmonary vessels occurs for a short time,
- (2) The recanalization of the reserve vessels and physiologic dilation of the standing vessels soon meet the increase,
- (3) Then, when at last the balance is lost the vessels dilate again unusually, and,
- (4) If that state continues the transudation begins, and then pulmonary edema is established.

Thus, for the development of pulmonary edema regardless of the inducing factors, the determinant role is always played by the breakdown of the balance between the pulmonary blood flow or volume and the reserve of the pulmonary vascular bed. Thinking of this it appears to be amount of conditions loaded rather than sort that matters primarily.

In pulmonary tuberculosis surgery every operation does essentially reduce the pulmonary vascular bed and every patient has the reserve vessels which have, more or less, already diminished before operation. Under such a situation, any other surplus unfavorable factor readily gives rise to the unbalance as above mentioned and works enough to induce pulmonary edema.

f) Electron microscopic evidence

It is easy to presume that a long lasting unusual dilation of the peripheral vessels brings about their rupture. We ascertained this by electron microscopic observation.

Under pulmonary edema the endothelial covering of capillaries loses its continuity, alveolar cells fall off detached from the endothelium, and the endothelial cells are vacuolated. These changes represent the very rupture of the vessels.

2) Reabsorption of the transudate

a) Absorption into blood vessels

After physiological saline solution containing P³² was injected into the alveolar spaces through the respiratory tract, absorption into blood vessels was measured in comparison with density in blood after intravenous injection. It was unexpectedly revealed that the physiological saline solution could be absorbed from

alveolar spaces as fast as in the case of intravenous injection.

This result, together with the fact that absorption into lymph canals takes place only so little, is thought to suggest that absorption of any liquid from alveolar spaces is performed chiefly through alveolar blood capillaries. On low oxygen or high CO₂ breathing the absorption diminishes temporarily, but when the load removed it increases again. This means that while the local changes are reversible liquid goes out or comes into the blood capillaries versatily. But when the local changes become of so high degree as to be irreversible the transudated liquid can no longer be absorbed into blood vessels even after the load is removed.

b) Absorption into lymph canals

Absorption of physiological saline solution into lymph canals much delays as compared with into blood vessels. It seems that in absorption of liquid in alveolar region lymph canals do not take almost any role in any instances. Lymph canals are available only in absorption of transudate in bronchioles proximal of the peripheral parts of terminal bronchioles and in the periarterial connective tissues. Altschule's theory, as previously mentioned, fails in the alveolar region just where pulmonary edema takes place.

IV. SUMMARY

In pulmonary tuberculosis surgery pulmonary edema is induced when the balance between the intrapulmonary blood flow or volume and the reserve of the pulmonary vascular bed comes to be broken. The former increases by anoxia, hypercapnia, blood transfusion, liquid infusion and so forth (extrinsic factors). The later decreases in pulmonary-diseased patients and after chest operation. (intrinsic factor).

As to the direct cause of acute pulmonary edema in pulmonary tuberculosis surgery we give a leading role to a decrease or extinction of the reserve vessels and the diminished dilatability of the peripheral vessels.

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